REMARKS

Claims 37-54 and 56-65 were pending and claim 60 was withdrawn. Claim 57 is cancelled by this amendment. Claims 37-40, 53, 56, 58, 59, and 62-65 are amended. New claim 66 is added. Support for the amendments and additions to the claims is found in the specification and claims as originally filed. For example, support for the amendments to claim 37 is at p. 8, ¶ 2; p. 10, line 3; p. 12, lines 11-15 and lines 24-27; support for claim 56 is at p. 8, last full paragraph; support for claim 63 is at p. 3, ¶ 4 and at p. 12, lines 24-27, and in previous claim 57; and support for new claim 66 is at page 7, last paragraph. Claim 38 has been amended to clarify that the protein repellant molecule is a hydrophilic polymer and to delete the reference to self assembled monolayers which has been incorporated into claim 37. Claim 40 has been amended to correct antecedent basis. Claim 53 has been amended to correct a typographical error. Claims 58 and 62 have been amended to correct the spelling of "spectrometry." Minor amendments have been made to claims 59, 64, and 65 to improve the clarity of the claims. No new matter is introduced by these amendments.

Rejections under 35 U.S.C. § 102(b)

Claims 37, 39, 54, 57, 59, 62, and 63-65 were rejected as anticipated by Nelson, *Mass Spec. Rev.* 16:353-376 (1997) ("Nelson"). Claim 57 has been cancelled. Applicants traverse with respect to the remaining claims, as amended.

Nelson does not teach a probe surface having a layer resistant to non-specific protein binding according to amended claim 37. Claim 37 requires the probe surface to comprise protein repellent molecules selected from the group consisting of hydrophilic polymers and self assembled monolayers. Accordingly, Nelson fails to anticipate claim 37 because it does not teach each and every element of the claim. Claims 39, 54, 59, 62, and 63-65 depend from claim 37 and therefore the rejection fails with respect to these claims for the same reasons.

Applicants request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 37-54, 56-59, and 61-65 were rejected as unpatentable over PCT International Application Publication No. WO 00/04382 ("Wagner") in view of U.S. Patent No. 6,258,538 ("Koster"). Claim 57 has been cancelled. Applicants traverse with respect to the remaining claims, as amended.

Wagner does not teach protein microarrays for use in mass spectrometry, nor does Wagner teach mass spectrometry probes coated with a layer resistant to non-specific protein binding according to claim 37. There is no teaching or suggestion in Wagner as to how mass spectrometry could be used to measure enzyme catalysis on protein microarrays. At most, Wagner teaches an assay for caspase activity that utilizes fluorescence detection. Accordingly, Wagner does not provide an expectation of success for using mass spectrometry to determine an enzyme's activity according to the claims.

Koster does not overcome the deficiencies of Wagner. Koster teaches the use of mass spectrometry for detecting particular nucleic acid molecules and sequences within those molecules. *See e.g.*, Abstract of Koster. But Koster does not teach a method for determining enzyme activity using mass spectrometry, nor does Koster teach a mass spectrometry probe coated with a layer resistant to non-specific protein binding according to claim 37. The Examiner relies on Koster for its teaching of ammonium carbonate buffer. Office action at p. 4, ¶¶ 3-4. This teaching does not render obvious the method of claim 37, either alone or in combination with the teachings of Wagner.

Thus, neither Wagner nor Koster teaches or suggests a method for determining enzyme activity using mass spectrometry in which the probe is coated with a layer resistant to non-specific protein binding according to claim 37. Further, in view of the lack of specific guidance in Wagner regarding how to use a protein microarray in combination with mass spectrometry to determine an enzyme's activity, and the lack of any teaching at all in Koster regarding the use of mass spectrometry to determine enzyme activity, the skilled person would neither arrive at the claimed invention by combining the cited references nor have a reasonable expectation of success in practicing the claimed method based on these references.

In summary, the Examiner has failed to establish a *prima facie* case of obviousness with respect to claim 37 and its dependent claims. Applicants request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 37-54, 56-59, and 61-65, were rejected for overbreadth. Office action at p. 6, ¶ 1. Claim 57 has been cancelled. Applicants traverse with respect to the remaining claims, as amended.

The Examiner contends that the specification at page 12 only broadly and insufficiently describes the claimed layer, stating as an example that polyethylene glycol with a functional group that may be attached via a linker encompasses a plethora of different compounds. Office action at p. 8, ¶ 1.

Claim 37 is directed to a method of determining an enzyme's activity or the activity of a G-protein coupled receptor by using mass spectrometry. The claim further requires that the probe surface have a layer resistant to non-specific protein binding comprising protein repellent molecules, wherein the protein repellent molecules are selected from hydrophilic polymers and self assembled monolayers immobilized on the probe surface.

The specification provides that the protein repellant molecules which make up the layer can be bound to the probe surface via a linker, such as a polyamino acid, and that the amino or carboxyl side groups of the linker can be used to bind the protein repellant molecules and/or the enzyme so that each extends out from the surface. Specification at p. 12, ¶¶ 1, 3. In a specific example, the protein repellant molecule is polyethylene glycol. Applicants submit that it is within the routine skill of the art to determine how to attach polyethylene glycol, or any of the other examples of protein repellant molecules listed at page 12, to the probe surface, a linker and/or an enzyme. All that is required is routine chemistry. It is well settled that the specification need not describe that which is well known in the art.

In view of the above, Applicants submit that the specification provides sufficient description of the claimed methods to enable the skilled person to practice it with a reasonable expectation of success. Accordingly, the enablement requirements of 35

U.S.C. § 112 are met and Applicants request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 37-54, 56-59, and 61-65 were rejected as indefinite. Claim 57 has been cancelled. Applicants traverse with respect to the remaining claims as amended.

Applicants have amended the claims to address the various informalities noted by the Examiner. In particular, claim 37 has been amended to provide antecedent basis for "activity" and "surface". This claim has also been amended to delete previous line (ii). Claim 37 has additionally been amended to specify protein repellant molecules.

Claim 38 no longer recites "self-assembled monolayers", and claim 39 has been amended to delete "such as". Claim 40 has been amended to provide proper antecedent basis for "one or more kinases". Claims 61 and 65 have additionally been amended to correct informalities noted by the Examiner.

Applicants traverse the rejection to the extent the Examiner asserts claims 39 and 65 are indefinite for reciting the term "ATP-dependent chaperone" in claims 39 and 65. First, an "ATP-dependent chaperone" is within the meaning of "enzyme" as articulated in the specification. *See e.g.*, the specification at p. 8, ¶ 1. Second, ATP-dependent chaperones can have inherent ATPase activity and thus are enzymes according to the standard usage of the term. In support, Applicants point to Prodromou, C. *et al.*, *EMBO J.* 18:754-762 (1999) (submitted in a Supplemental IDS filed concurrently with this response) which refers to "... the inherent ATPase activity of Hsp90" (see abstract); and Lee, S. and Tsai, F.T.F., *J. Biochem. M. Biol.*, 38:259-265 (2005) (submitted herewith) which teaches that ATPases function as molecular machines by converting metabolic energy in the form of ATP into mechanical work (see page 259, col. 2, ¶ 2). Accordingly, claim 37 is not indefinite for reciting "ATP-dependent chaperone".

Applicants request reconsideration and withdrawal of the rejections for indefiniteness.

Applicants submit that the application is in condition for allowance and request an action for same. A Petition for Extension accompanies this response. Please charge any additional fees that may be due, or credit any overpayment, to Deposit Account No. 50-0311, Attorney Reference No. **40418-509N01US**.

Respectfully submitted,

Date: April 2, 2010

David Johnson, Reg. No. 41,874
Attorney for Applicants
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623